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Clinical outcomes of the omicron variant compared with previous SARS-CoV-2 variants; meta-analysis of current reports

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Abstract

BACKGROUND

Omicron (B.1.1.529) is a new SARS-CoV-2 variant of concern; however, there is no comprehensive analysis regarding clinical features, disease severity, as well as clinical outcomes of this variant.

AIM

This study was a comprehensive review and statistical analysis on the comparison between clinical characteristics of infection with Omicron variant and previous variants.

METHODS

We searched major international databases consisting ISI Web of Science, PubMed, Scopus, and MedRxiv to collect the potential relevant documents. Finally, clinical features *e.g.* death rate, ICU admission, length of hospitalization stay, and mechanical ventilation of Omicron variant compared with previous COVID-19 waves were assessed using odds ratio (OD) corresponding 95% confidence intervals (CI) by Comprehensive Meta-Analysis (CMA) software version 2.2 (Biostat, Englewood, NJ, USA).

RESULTS

A total of 12 articles met our criteria; these articles had investigated the clinical outcomes of Omicron variant compared with other variants such as alpha, beta, and delta. Our results suggested that ICU admission, need to mechanical ventilation, and death rate was significantly lower in Omicron than previous variants. In addition, the average length of hospitalization stay during Omicron wave was meaningfully shorter than other variants.

CONCLUSION

The infectivity of Omicron variant was extremely higher than previous variants due to the presence of several mutations particularly in spike protein. However, disease severity in Omicron variant was mild to moderate disease compared than previous waves.

INTRODUCTION

Coronavirus disease 2019 (also known as COVID-19) is a global pandemic that first emerged from Wuhan, China in December 2019. According to the World Health Organization (WHO) reports, there are more than 378 million cases, as well as 5.67 million deaths due to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (1). On 24 November 2021, the Network for Genomics Surveillance in South Africa (NGS-SA) reported a new variant of this virus named Omicron (B.1.1.529) from Gauteng Province and South Africa that was confirmed by WHO on 25 November 2021 (2, 3).

The Omicron variant rapidly replaced the previous variants in South Africa and spread to other countries, so it quickly became a dominant variant. In the United States, approximately 95% of all SARS-CoV-2 new cases were diagnosed as the Omicron variant by January 2022 (4, 5).

The genome of this variants carries 26-32 mutations in spike gene as well as 45-52 amino acid substitutions which are associated with increased transmissibility, immune escape,

and “S gene target failure” (SGTF); SGTF is due to the 69 to 70 deletion in the S gene of B.1.1.7 (6-8). Early studies have documented the inefficacy of current vaccines (vaccination schemes and booster doses) and the higher rate of re-infection with the Omicron variant (9, 10). Based on animal model findings, the severity of symptoms as well as the viral load in the Omicron variant was lower compared to the previously reported variants of SARS-CoV-2 (11, 12). Clinical reports from Scotland, England, Canada, and United States have also confirmed animal experiments (13-16). However, the fourth global wave of SARS-CoV-2 caused by the Omicron variant was not associated with increased hospitalization or death in comparison with previous SARS-CoV-2 outbreaks (17).

Understanding the clinical characteristics, susceptibility factors, and immune response against the new SARS-CoV-2 variants could be a useful strategy for the establishment of infectious control programs and the development of novel therapeutic options. In the current report, we evaluated the clinical severity of Omicron variant compared to previous SARS-CoV-2 variants.

MATERIALS AND METHODS

We searched in global databases such as ISI Web of Science, PubMed, Scopus, and MedRxiv using keywords according to MeSH terms such as “Omicron”, “COVID-19”, “SARS-CoV-2”, “Disease severity”, “Variant of concern”, “ICU”, “Intensive care unit”, and “fourth wave” by February 2022. Then we retrieved all potential studies related to the clinical severity of Omicron regardless limitation in language and publication date. All eligible documents were carefully screened; required data including mean age, immunization status, mortality rate, ICU admission, length of hospitalization stay, and mechanical ventilation are summarized in Table 1.

Table 1: Characteristics of included studies

We also reviewed the documents’ bibliography to avoid missing relevant articles. Finally, the disease severity of Omicron compared to previous SARS-CoV-2 waves was evaluated using the odds ratio (OR) corresponding 95% confidence intervals (CI). We

used random-effect size due to the presence of significant heterogeneity (I-squared index and Cochrane *p* value test). Data were pooled using Comprehensive Meta-Analysis (CMA) software version 2.2 (Biostat, Englewood, NJ, USA).

RESULTS

A total of 12 articles had investigated the clinical outcomes of the Omicron variant compared to other variants *e.g.* alpha, beta, and delta. Eligible studies were performed in South Africa, the United States, Portugal, the United Kingdom from 2021 to 2022 (18-29). We pooled the data on 887,132 molecular confirmed SARS-CoV-2 cases including 163,457 Omicron variants as well as 723,675 other SARS-CoV-2 variants.

The mean age of patients infected with Omicron variant was 28.93 ± 15 years. The frequency of events such as ICU admission, need to mechanical ventilation, and death rate for B.1.1.529 variant was at 0.8% (95%CI: 0.2-3.7; I^2: 99.89; *p* value: 0.01; Egger's *p* value: 0.01; Begg's *p* value: 0.29), 0.2% (95%CI: 0.1-0.5; I^2: 95.75; *p* value: 0.01; Egger's *p* value: 0.16; Begg's *p* value: 0.26), and 0.4% (95%CI: 0.1-1.0; I^2: 98.47; *p* value: 0.01; Egger's *p* value: 0.01; Begg's *p* value: 0.45), respectively. The average length of hospitalization stay during the Omicron wave was 3.36±1 days. Also, the incidence of Omicron infection among fully vaccinated individuals was 12.9% (95%CI: 5-27; I^2: 99.89; *p* value: 0.01; Egger's *p* value: 0.22; Begg's *p* value: 0.40). the current findings revealed that the severity of infections caused by Omicron reassuringly is less than previous infections caused by alpha, beta, and delta variants; the current findings is consistent with similar reports (30, 31).

In comparing the fourth wave caused by the Omicron variant with previous waves, it should be said that the mean age for Omicron was about 13 years (28.93±15) less than that for other variants (41.29±17). There was a significant reduction in ICU admission (OR: 0.18; 95%CI: 0.094-0.37; *p* value: 0.01; I^2: 99.05; *p* value: 0.01; Egger's *p* value: 0.2; Begg's *p* value: 0.07) (Figure 1).

Fig. 1. Forest plot of the meta-analysis on ICU admission of SARS-CoV-2 Omicron variant.

Our results suggested a significant reduction in the need for mechanical ventilation (OR: 0.135; 95%CI: 0.05-0.31; p value: 0.01; I^2: 97.24; p value: 0.01; Egger's p value: 0.12; Begg's p value: 0.26) among Omicron cases (Figure 2).

Fig. 2. Forest plot of the meta-analysis on the need to mechanical ventilation in cases infected with SARS-CoV-2 Omicron variant.

Furthermore, the mortality rate was also declined among patients infected with Omicron variant (OR: 0.17; 95%CI: 0.06-0.46; p value: 0.01; I^2: 98.32; p value: 0.01; Egger's p value: 0.44; Begg's p value: 0.71) compared to previous variants (Figure 3).

Fig. 3. Forest plot of the meta-analysis on risk of mortality of SARS-CoV-2 Omicron variant.

DISCUSSION

Also, the average length of hospitalization stay in Omicron was significantly less than other variants (3.36 ± 1 days for Omicron *vs*. 7.98 ± 3 days for other variants; p value < 0.05). In summary, we found that the disease severity of the Omicron variant was significantly less than other previous waves; however, there was significant heterogeneity that could be due to differences in several factors such as study design, geographical region, time for the assessment of clinical outcomes, and diverse condition of included cases; publication bias was also significant. Recently, Zhao *et al*, showed that the Omicron variant is less dependent to TMPRSS2 mediated entry-pathway that leads to less efficient replication and decrease viral load within the human lungs (32). In addition, the Omicron variant is more susceptible to interferons than other variants,

especially the delta variant (33). Similar evidence could be a reasonable explanation for the lower severity of the Omicron variant, as confirmed by numerous observational studies (15).

The Omicron variant nucleotide sequence has several mutations, especially 32 single substitutions in spike protein that cause persistence to neutralizing antibodies (Nab) as well as inefficiency of current vaccines (34-36). We revealed that Omicron variant has less severity than previous variants; however, heterogeneity and publication bias were significant in our estimations (Figure 4). Further studies need to confirm the present findings.

Fig. 4. Funnel plot of the meta-analysis on disease severity of Omicron variants compared than previous SARS-CoV-2 variants.

CONCLUSION

Conclusively, a new global increase in SARS-CoV-2 patients is accompanied with the emergence of the Omicron variant that is associated with less severity in disease, as well as fewer ICU admission, hospitalization stay, and mortality rate. Nonetheless, there is limited information about the effect of Omicron on pediatrics, pregnant women, and immunodeficient individuals. Overall, Omicron has been considered as the most contagious SARS-CoV-2 variant that affects children and young adults more than other groups. Continuation of the current situation can have deadly consequences for these age groups.

ARTICLE HIGHLIGHTS

Research background

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Omicron (B.1.1.529) is a new SARS-CoV-2 variant of concern; however, there is no comprehensive analysis regarding clinical features, disease severity, as well as clinical outcomes of this variant.

Research motivation

there is no sufficient evidence regarding clinical characteristics, standard therapeutic regimen, as well as efficacy of current available vaccines against omicron variant.

Research objectives

This study was a comprehensive review and statistical analysis on the comparison between clinical characteristics of infection with Omicron variant and previous variants.

Research methods

We searched major international databases consisting ISI Web of Science, PubMed, Scopus, and MedRxiv to collect the potential relevant documents. Finally, clinical features *e.g.* death rate, ICU admission, length of hospitalization stay, and mechanical ventilation of Omicron variant compared with previous COVID-19 waves were assessed using odds ratio (OD) corresponding 95% confidence intervals (CI) by Comprehensive Meta-Analysis (CMA) software version 2.2 (Biostat, Englewood, NJ, USA).

Research results

A total of 12 articles met our criteria; these articles had investigated the clinical outcomes of Omicron variant compared with other variants such as alpha, beta, and delta. Our results suggested that ICU admission, need to mechanical ventilation, and death rate was significantly lower in Omicron than previous variants. In addition, the average length of hospitalization stay during Omicron wave was meaningfully shorter than other variants.

Research conclusions

The infectivity of Omicron variant was extremely higher than previous variants due to the presence of several mutations particularly in spike protein. However, disease

severity in Omicron variant was mild to moderate disease compared than previous waves.

Research perspectives

Although we revealed that the disease severity of Omicron was lower than previous variants. However, this variant was more contagious. Nevertheless, further investigation with larger samples need to confirm the present findings.

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